An Ontological Representation of Adverse Drug Events

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Motivation

• Adverse drug events (ADE) are a well-recognized cause of patient morbidity and increased health care costs in the United States.

• Multiple studies have demonstrated that a clinical decision support (CDS) system based on a standardized ADE knowledge base can be useful to help physicians reduce the risk of their patients’ medications.
ADEpedia – A scalable and standardized knowledge base of ADEs

• To propose a comprehensive framework for building a standardized Adverse Drug Event knowledge base (called ADEpedia) through combining ontology-based approach with semantic web technology.

• To implement a prototype to demonstrate the capability of the system which integrates multiple ontology resources and open web services for the ADE data standardization.
Objective of the study

• We describe our preliminary effort on development of an ontological representation pattern for the ADE domain.

• We discuss clinical implications of the effort and potential challenges with respect to its integration with existing data standards.
ADEpedia framework

1. SPL Labels (XML) - Terminology Mapping
2. XML2RDF Transformer (Syntax) - Standardized Terminologies (RxNorm, SCT, MedDRA...)
3. Standards for Interoperability W3C XML/RDF, HL7, CDA...
4. Standardized Adverse Drug Events RDF Store

Frontend For Review/Curation (Semantic MediaWiki)
Knowledge Resources

• To build the ADE knowledge base, we utilized three different resources, comprising of
  • 1) the drug information resource from all available Structured Product Labels;
  • 2) the standard drug ontology RxNorm and its service API at RxNAV;
  • 3) the standard clinical terminologies SNOMED CT and MedDRA for the ADE annotations through the NCBO BioPortal OBA annotation web service.
Linkage between Drugs and ADEs

• We successfully linked the ADEs coded by SNOMED CT and MedDRA with the drug ontology RxNorm.

• For example, using a SPAQL query, we identified 28 distinct RxNorm drugs linked with the ADE “Prolonged QT interval” represented by a SNOMED CT code “111975006” and the ADE “QT prolonged” represented by a MedDRA code “10037705”
Problems on knowledge representation

• However, there is no standardized, controlled vocabulary available that allows the ADE information to be described in an unambiguous way in such a knowledge base.

• An ontological representation of the ADE domain would provide computable semantics for an ADE knowledge base, and facilitate semantic integration of ADE related data standards.
ADEpedia Domain Pattern

Adverse Drug Effect Class

has_member

is_member_of

Drug Class

has_member

is_member_of

Adverse Drug Effect

may_be_induced_by

Medication

may_induce

may_induce
<table>
<thead>
<tr>
<th>Relation Definition</th>
<th>RDF Schema</th>
</tr>
</thead>
</table>
| **may_induce**      | `<adepedia:may_induce> a <rdf:Property>;
  <rdfs:domain> <adepedia:Meciation>;
  <rdfs:range> <adepedia:AdverseDrugEffect> .` |
| **may_by_induced_by** | `<adepedia:may_by_induced_by> a <rdf:Property>;
  <rdfs:domain> <adepedia:AdverseDrugEffect>;
  <rdfs:range> <adepedia:Meciation> .` |
| **has_member**      | `<adepedia:has_member> a <rdf:Property>;
  <rdfs:domain> <adepedia:AdverseDrugEffectClass>;
  <rdfs:range> <adepedia:AdverseDrugEffect> .` |
| **is_member_of**    | `<adepedia:is_member_of> a <rdf:Property>;
  <rdfs:domain> <adepedia:AdverseDrugEffect>;
  <rdfs:range> <adepedia:AdverseDrugEffectClass> .` |
| **has_member**      | `<adepedia:has_member> a <rdf:Property>;
  <rdfs:domain> <adepedia:DrugClass>;
  <rdfs:range> <adepedia:Medication> .` |
| **is_member_of**    | `<adepedia:is_member_of> a <rdf:Property>;
  <rdfs:domain> <adepedia:Medication>;
  <rdfs:range> <adepedia:DrugClass> .` |
Table 2. The example instances in RDF Turtle format

_:b0 a <adepedia:AdverseDrugEffectClass>;
  <adepedia:code> "T45.515";
  <adepedia:displayName> "Adverse effect of anticoagulants";
  <adepedia:codeSystemName> "ICD-10-CM" .

_:b1 a <adepedia:DrugClass>;
  <adepedia:code> "C8812";
  <adepedia:displayName> "Anticoagulants";
  <adepedia:codeSystemName> "NDF-RT" .

_:b2 a <adepedia:Medication>;
  <adepedia:code> "114194";
  <adepedia:displayName> "Warfarin Sodium";
  <adepedia:codeSystemName> "RxNORM" .

_:b3 a <adepedia:AdverseDrugEffect>;
  <adepedia:code> "34436003";
  <adepedia:displayName> "Blood in urine";
  <adepedia:codeSystemName> "SNOMED CT" .
A Scalable and Standardized Knowledge Base of Adverse Drug Events

Run query: Medication Query By ADE

Type a string of adverse event name like "pain" below, select a value from a suggestion list and then click the "Run query" button; this search is to query the medications that may induce the selected adverse drug event.

Adverse
Drug
Event:

(This is a demonstration of the Query medication by ADE.)

Run query

http://adepedia.org
ADEpedia Domain Pattern

Adverse Drug Effect Class

has_member

is_member_of

Drug Class

has_member

is_member_of

Adverse Drug Effect

may_be_induced_by

Medication

may_induce

Gene

Protein

Pathway

....
Summary

• We identified and defined a domain pattern for the ADE knowledge representation.

• We consider this pattern can be a starting pointing for an ontological representation of ADE domain.

• We believe that a community-based effort would be required to achieve a comprehensive standardized ontology for the domain, which would facilitate the semantic interoperability of the ADE knowledge bases in heterogeneous CDS systems and ultimately improve patient safety.
Questions & Discussion